

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION

See paragraph 2 below

International application No.
PCT/EP2004/011952

International filing date (day/month/year)
20.10.2004

Priority date (day/month/year)
22.10.2003

International Patent Classification (IPC) or both national classification and IPC
C07C311.08, C07C235.42, C07C217.54, C07D213.65, A61P11.08, A61K31/166, A61K31/18, A61K31/44

Applicant
GLAXO GROUP LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

Box No. II Priority

1. ☒ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43*bis*.1 and 64.1) is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
☒ claims Nos. 11

because:

- ☒ the said international application, or the said claims Nos. 11 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
- | | |
|----------------------------|--|
| the written form | <input type="checkbox"/> has not been furnished |
| | <input type="checkbox"/> does not comply with the standard |
| the computer readable form | <input type="checkbox"/> has not been furnished |
| | <input type="checkbox"/> does not comply with the standard |
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/011952

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	3-4, 10-15
	No: Claims	1,2, 5-9, 16
Inventive step (IS)	Yes: Claims	3-4, 10-15
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-10, 12-16
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

Re Item III.

Claim 11 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V.

1 Reference is made to the following documents

D1: EP-A1-0 239 815 (THOMAE, DR. KARL, G.M.B.H., FED. REP. GER.) 7
October 1987 (1987-10-07)

D2: EP-A1-0 198 412 (HOFFMANN-LA ROCHE, F., UND CO. A.-G., SWITZ.) 22
October 1986 (1986-10-22)

D3: US-A-4 992 474 (SKIDMORE ET AL) 12 February 1991 (1991-02-12)

- 2.a) The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1, 2, 5-9 and 16 is not new in the sense of Article 33(2) PCT (see the compound on column 8, lines 22-26, which is used as starting compound for the preparation of the compound of example 12. Said compound has been disclosed in D2 merely as intermediate for the preparation of the active compounds of formula (I) of D2 without any reference to pharmacological properties. Therefore, the subject-matter of claims 3-4 and 10-15 is considered to be novel vis-à-vis D2.
- b) Claim 1 of the present application can be considered to be novel vis-à-vis D1, mainly on account of the fact that the substituent Ar¹ does not represent a thiazole or oxazole group (Art. 33(2)PCT).
- c) Claim 1 of the present application can be considered to be novel vis-à-vis D3, mainly on account of the fact that:

the moiety $(CH_2)_k$ is not linked to the phenyl group through an oxygen atom

the presence of the proviso "that in the group (a), when R^{11} represents $-(CH_2)_nOR^{15}$ and n is 1, R^{13} is not OH".

the presence of the moiety $-O(CH_2)_mZ(CH_2)_pCR^aR^bPh(R^1)(R^2)(R^3)$

3. The closest prior art is considered to be D3 which also discloses phenethanolamine derivatives useful as agonists at the β_2 -adrenoreceptors.

The problem underlying the invention is considered to be the provision of further compounds useful as agonists at the β_2 -adrenoreceptors.

The present compounds differ from the compounds disclosed in D3 as mentioned above (see V.2(c)) and are therefore not considered as obvious structural analogues of the compounds disclosed in D3. Therefore, the subject-matter of the present application is considered to fulfil the requirements of Art. 33(3)PCT.

- VI. D4: WO 03/091204 A1 (GLAXO GROUP LIMITED, UK) 6 November 2003 (2003-11-06)

- D5: ALIKHANI, VAHID ET AL: "Long-chain formoterol analogues: an investigation into the effect of increasing amino-substituent chain length on the β_2 -adrenoceptor activity" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, 14(18), 4705-4710 CODEN: BMCLE8; ISSN: 0960-894X, 2004, XP002323505

For the purposes of this report it has been considered that the priority date (22/10/03) of the present application has been validly claimed. If this were not the case, D4 and D5 could become relevant at the regional phase.

The subject-matter of the present application is novel vis-à-vis D4 on account of the proviso "that in the group (a), when R^{11} represents $-(CH_2)_nOR^{15}$ and n is 1, R^{13} is not OH".